

REMARKS

Reconsideration of the application as amended is respectfully requested.

Pursuant to 37 C.F.R. § 1.136(a), Applicants hereby request a two month extension of the term for reply set by the August 30, 2001 Office Action, i.e., up to and including January 30, 2002. Enclosed herewith is a check for a two month extension of time (\$400.00) to respond to an official action for a large entity. The Commissioner is authorized to charge any additional fees to Deposit Account No. 50-0320.

Claims 1-14 and 18-24 are pending. Claims 15-17 are cancelled with prejudice. Claims 2, 3, and 6-14 are amended and new claims 18-24 are added without prejudice. Support for the amended claims and new claims can be found throughout the specification.

Claims 9-14 are objected to as allegedly being in improper form. Applicants respectfully submit that claims 9-14 were amended in the preliminary amendment filed January 2, 2001, thereby rendering the claim objection moot.

With regard to the Examiner's assertion that it is not clear when x-y represents  $-\text{CH}_2\text{CH}-$  OP, what is connected to the  $\text{C}(\text{CH}_3)_2\text{C}=\text{O}$ , Applicants respectfully submit that a skilled artisan would understand that it is the CH that is connected to the  $\text{C}(\text{CH}_3)_2\text{C}=\text{O}$  group. Further a skilled artisan would understand that oxygen cannot form a bridge to the  $\text{C}(\text{CH}_3)_2\text{C}=\text{O}$  group because the oxygen atom is linked to the carbon atom of the  $\text{CH}_2\text{CH}$  group. Therefore further clarification is not necessary and the rejection should be withdrawn.

Claims 1-17 are rejected under 35 U.S.C. §112 second paragraph as being allegedly indefinite. The rejection is traversed.

Claims 6-16 are amended to delete the recitation "characterized in" rendering this rejection moot.

Claim 2 is amended to recite that B is boron thereby obviating the rejection.

Claims 9-14 are amended to recite a "process for the preparation of a compound" rendering this rejection moot.

Claim 3 is amended to recite that Hal is a halogen especially Br or I thereby obviating the rejection.

Claims 15-17 are cancelled rendering the rejection moot.

Claims 4, 5, 7 and 8 are rejected under 35 U. S. C. §102(b) as being allegedly anticipated by Nicolaou et al. (Chem. Eur. J., 3(12):1971-1986, 1997).

The Examiner alleges that Nicolaou et al. discloses total synthesis of oxazole- and cyclopropane-containing epothilone B analogues by the macrolactonization approach. The Examiner further alleges that the compounds no.2 and 30-32 disclosed by Nicolaou anticipate the instant claims when X-Y represent  $\text{CH}_2\text{CH-OP}$  and  $\text{R}_2$  represents a monocyclic heteroaryl group in the instant compounds of formula (6).

The present invention is directed to *inter alia*, epothilone derivatives, process for preparing epothilone derivatives, pharmaceutical compositions comprising epothilone derivatives and a method of protecting plants using epothilone derivatives.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Bariant Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Applying the law to the instant facts, Nicolaou et al. does not disclose, suggest or enable Applicants' invention. Nicolaou et al. does not contain all of the elements of the instant claims, e.g., X-Y, a group of the formula  $-\text{CH}_2\text{CH-OP}$  or  $\text{CH}=\text{CH-}$ , and P= a protective group. Accordingly, the Examiner failed to meet his burden in showing that Nicolaou et al. contains every limitation of the rejected claims. There is no teaching or suggestion of the epothilone derivatives containing a protective group as described in the present invention.

In view of the foregoing, reconsideration and withdrawal of the rejection under 35 U.S.C. Section 102 is respectfully requested. Therefore, there is no teaching, suggestion, or motivating recitation in either of the references that would lead a skilled artisan to practice the instantly claimed invention.

Consequently, reconsideration and withdrawal of the rejection under Section 103 is respectfully requested.

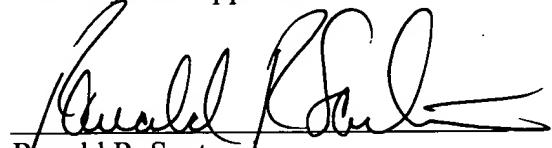


Applicants wish to note that included herewith is a change of correspondence address for this application.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP  
Attorneys for Applicant

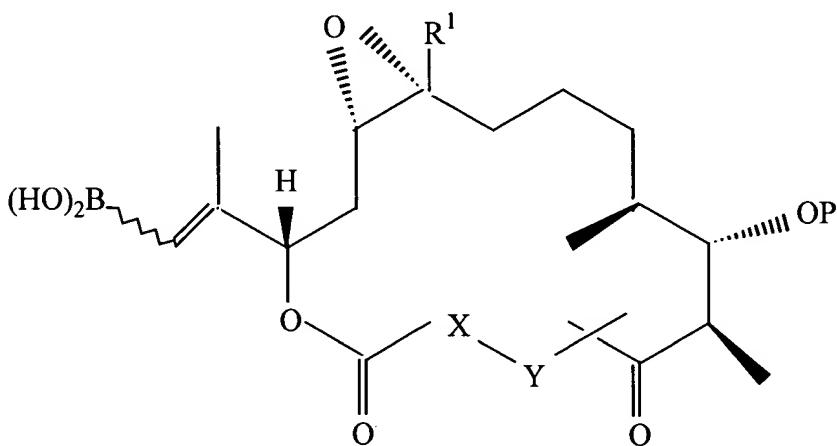
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APPENDIX 1:VERSION TO SHOW CHANGES MADE

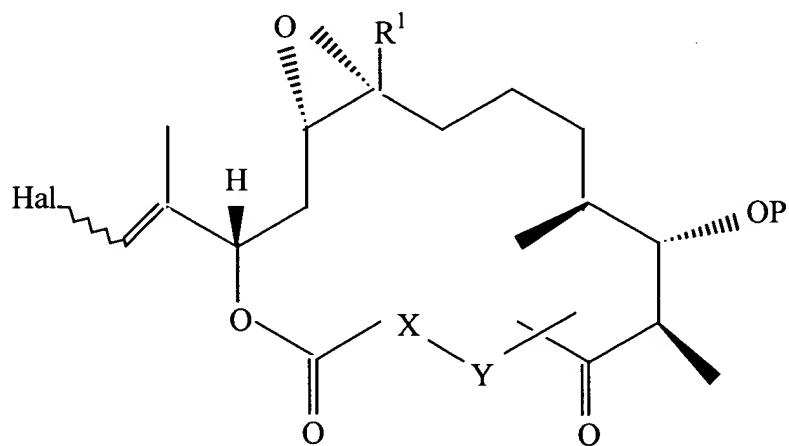
IN THE CLAIMS:

2. (Amended) Epothilone derivative of formula (3)



wherein B is boron and the residues are as defined in claim 1.

3. (Amended) Epothilone derivative of formula (4)



wherein the residues  $R^1$ , X-Y and P are defined as in claim 1, and Hal is a halogen [such as] especially Br or I.

6. (Amended) Epothilone derivative according to claim 1, [characterized in that] wherein  $R^1$ ,  $R^4$ ,  $R^5$  and  $R^6$  are a hydrogen atom or a C<sub>1-6</sub>-alkyl group, especially a C<sub>1-6</sub>-alkyl group.

7. (Amended) Epothilone derivative according to claim 4, [characterized in that] wherein the substituents of the monocyclic aromatic and/or hetero aromatic are C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-alkenyl and C<sub>2-6</sub>-alkinyl groups respectively, especially C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-akinyl groups, respectively and the halogen atoms fluoro, chloro, bromo or iodo atoms.

8. (Amended) Epothilone derivative according to claim 4, [characterized in that] wherein the aromatic and hetero aromatic, respectively, is provided with 1, 2 or 3 substituents and the hetero aromatic is provided with 1, 2 or more and especially 1, 2, 3, or 4 hetero atoms.

9. (Amended) Process for the [production] preparation of a compound of formula (3), [characterized in that] wherein a compound of formula (2) is reacted with the compound of formula HC [B (OR)<sub>2</sub>]<sub>3</sub> [if wanted] optionally in the presence of a base, wherein the residues are defined as in claim 1 and R is defined as R<sup>1</sup>, but is independent of R<sup>1</sup>.

10. (Amended) Process for the [production] preparation of a compound of formula (4), [characterized in that] wherein a compound of formula (3) is reacted with N-iodo- or N-bromo succinimide and that the residues are defined as in claim 1.

11. (Amended) Process for the [production] preparation of a compound of formula (5), [characterized in that] wherein a compound of formula (3) is reacted by a Suzuki coupling with a compound of formula R<sup>2</sup>-Z, wherein R<sup>2</sup> is defined as in claim 1 and Z can be a halogen atom or a group of formula -OSO<sub>2</sub>CF<sub>3</sub>, -CH=CHI, -CH=CHOSO<sub>2</sub>CF<sub>3</sub>.

12. (Amended) Process for the [production] preparation of a compound of formula (5),  
[characterized in that] wherein a compound of formula (4) is reacted by a silent coupling (stille  
Kupplung) with R<sub>2</sub>-SNR<sup>3</sup><sub>3</sub>, wherein R<sup>2</sup> is defined as in claim 1 and R<sup>3</sup> is a C<sub>1-6</sub>-alkyl group,  
especially a C<sub>1-4</sub>-alkyl group, preferably a methyl, ethyl, propyl or butyl group.

13. (Amended) Process for the [production] preparation of a compound of formula (6),  
[characterized in that] wherein the protective group is removed from a compound of formula (5).

14. (Amended) Process for the [production] preparation of a compound of formula (6),  
[characterized in that] wherein it comprises the process steps as disclosed in claim 9.